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Occurrence, fate and removal efficiencies of pharmaceuticals in wastewater treatment plants (WWTPs) discharging in the coastal environment of Algiers

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ABSTRACT

In the last few decades, the presence of pharmaceutical products in the environment is known under the name of emerging contaminants. These substances can enter the aquatic environment via different sources, as parent compounds, metabolites or a combination of both. In this work, we have investigated the presence of four pharmaceutical active compounds belonging to the group of Non-Steroidal Anti-Inflammatory Drugs (NSAIDs), in wastewater, surface water and drinking water of Algiers, which have a direct impact on the Mediterranean Sea. The target analytes (ibuprofen (IBU), naproxen (NAP), ketoprofen (KET), and diclofenac (DIC)), were extracted from the water samples by using Solid Phase Extraction Oasis® HLB Cartridges; the identification and quantification were realized by Gas Chromatography–Mass Spectrometry (GC–MS). To obtain the best resolution and precision, *N*-methyl-*N*-(trimethylsilyl) trifluoroacetamide (MSTFA) was used as the derivatization reagent and ibuprofen-d_3 was used as the internal standard. The obtained recoveries were good, ranging from 82% for ketoprofen to 120% for naproxen with relatively small standard deviations ($\leq$20%). The target compounds were detected in wastewater, influent/effluent with concentrations ranging from 155.5 to 6554 ng/L, implicating removal efficiencies of wastewater treatment plants (WWTPs), between 30.3 and 95%. The surface water was also contaminated with pharmaceuticals from 72.9 ng/L for diclofenac to 228.3 ng/L for naproxen. In addition, the occurrence of ibuprofen and ketoprofen in drinking water, at concentrations of 142.1 and 110.9 ng/L, respectively, attracts concerns about possible impacts on human health.

1. Introduction

The water quality is indispensable for the ecosystem's health and human life. Its pollution has been the subject of many studies in the last few years. In Algeria, pollutants such as pesticides, polychlorinated biphenyls (PCBs), heavy metals and poly aromatic hydrocarbons (PAHs) were studied and discussed in many research papers [1,2].

The presence of pharmaceutical products in the aquatic environment is considered by the scientific community as a new source of pollution. The production and use of pharmaceuticals and personal care products (PPCPs) have considerably increased during the last few decades, thus attracting worldwide attention. In the European Union

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(EU), around 3000 different pharmaceutically active compounds (PhACs) have been approved for use in medicines for humans. However, their potential impacts on the environment are less understood and have become the focus of global environmental researchers' studies [3,4].

Pharmaceutical products are discharged in the environment through industrial and domestic wastewaters without any restriction. The occurrence of some 160 pharmaceuticals has been confirmed [5]. Moreover, many studies have confirmed the presence of these compounds in different aquatic systems either as parent compounds and metabolites or the conjugates of both [6–12]. However, the prohibition or restriction of many PPCPs, which became indispensable in human's live, is unreasonable.

Non-steroidal anti-inflammatory drugs (NSAIDs) are among the most frequently detected pharmaceuticals in wastewaters, surface waters, ground waters and even in drinking waters because of their high consumption. They are generally used without prescription and their widespread distribution in the aquatic systems is due to the hydrophilicity and stability of these molecules [13]. The most part of administered dose of these compounds can be excreted unmetabolized into wastewater and their elimination by the current style of Waste Water Treatment Plants (WWTPs) is not efficient enough [11,14].

Recent methods for the analysis and determination of pharmaceuticals in aqueous samples are widely based on gas chromatography coupled to mass-spectrometry (GC–MS or GC–MS/MS) or liquid chromatography coupled to mass spectrometry (LC–MS or LC–MS/MS). Liquid chromatography has the advantage of avoiding the additional derivatization step. However, a relatively expensive instrument, LC–MS may suffer from matrix effects mainly due to signal suppression and/or enhancement in electrospray ionization (ESI), and signal enhancement in atmospheric pressure chemical ionization (APCI), and reduced reproducibility, engendering relatively high limits of detection [15]. As an easy operation with low cost, GC–MS has been largely used in the analysis of PhACs in aqueous environment samples proving good selectivity, high sensitivity and less problems associated with matrix effects [8,15–18].

Solid-phase extraction (SPE) has replaced traditional liquid–liquid extraction (LLE) and become the most common sample preparation technique to extract pharmaceuticals from environmental waters. Conventional C18 columns showed limited recovery for polar compounds. Oasis® HLB (hydrophilic–lipophilic balanced) was produced to overcome this problem and it remains as the cartridge of choice for the pre-concentration of both polar and non-polar compounds using the same extraction conditions [19].

Due to their weak volatility, high polarity and thermal fragility, NSAIDs need a derivatization step (organic reactions: methylation, silylation, or acetylation) to improve their GC resolution. Silyl reagents are widely applied for PhACs containing hydroxyl or carboxyl functional groups. The most used reagents are *N*-(*tert*-butyldimethylsilyl)-*N*-methyl-trifluoroacetamide (MTBSTFA) [15,20], *N*-methyl-*N*-(trimethylsilyl) trifluoroacetamide (MSTFA) [8,16,21] and bis(trimethylsilyl) trifluoroacetamide (BSTFA) [18,22].

Our objective in the present study is to search the presence of four acidic pharmaceutical active compounds (NSAIDs), frequently encountered in drinking water, surface water, WWTP influents and effluents received by the Mediterranean Sea around Algiers (Algeria). The analytical method was based on SPE extraction followed by GC–MS analysis. An isotope-labelled internal standard was used to compensate the matrix effects as well as for the verification of accuracy and analytical method precision. To our knowledge, this study presents the first measurements of PhACs in wastewater, surface water and drinking water in Algiers.

2. Materials and methods

2.1. Chemicals and reagents

Pharmaceutical compounds used are ibuprofen (IBU), diclofenac (DIC), ketoprofen (KET), and naproxen (NAP). Isotope-labelled standard ibuprofen-d_3 (IBU-d3) and 1-Hydroxypyrene (HPY) were purchased from Sigma-Aldrich, both with purity higher than 98%. Na_2EDTA (99%), Ortho-phosphoric acid (85%), HPLC-grade methanol and ethyl acetate were provided by Sigma-Aldrich. Oasis® hydrophilic–lipophilic balanced (HLB, 3 cc, 60 mg) solid phase extraction cartridges were purchased from Waters (USA). GFF glass fibre filters, pore size 1.6 μm and Nylon filters, pore size 0.45 μm were from Filtres-Fioroni. MSTFA as the derivatization reagent was purchased from Sigma-Aldrich. Ultrapure water with a resistivity of 18.2 MΩ cm was obtained from a milli-Q system (Millipore).

Stock standard solutions were prepared at a concentration of 1 mg/mL by dissolving appropriate amounts of each drug in methanol. The stock solutions and mixtures were stored in the dark at −20 °C.

2.2. Sample collection

Influent and effluent water samples were collected during November 2014 at two wastewater treatment plants: The Beni Messous WWTP and Reghaia WWTP in Algiers. 24-h composite samples were collected for the raw influents and final effluents. Drinking water was directly collected in our laboratory as a manual composite sample of tap water from USTHB University, while for the surface water, grab samples were collected from the El-harrach valley (10 km east Algiers) in January 2015 (Fig. 1).

Water samples were collected in 1 L amber glass bottles, previously washed with detergent, rinsed with nitric acid, organic solvents (acetone and methanol) and UP-Water. They were finally heated at 150 °C during 8 h.

The samples were immediately filtered with 1.6 μm glass fibre filters and 0.45 μm nylon filters; the pH was adjusted at 2.5–3 with *ortho*-phosphoric acid 5% [23,24]. The samples were stored in darkness at 4 °C and extracted within 24 h.

The Reghaia WWTP is designed for 400,000 population equivalent with an average daily flow of 80,000 m^3/day. The nature of waters treated in this WWTP is Mixed Wastewaters (domestic and industrial). It discharges the treated water into Reghaia Lake and finally in the Mediterranean Sea. The Beni Messous WWTP serves 250,000 inhabitants with an average daily flow of 50,400 m^3/day. It treats mainly domestic sewage, employing mechanical and

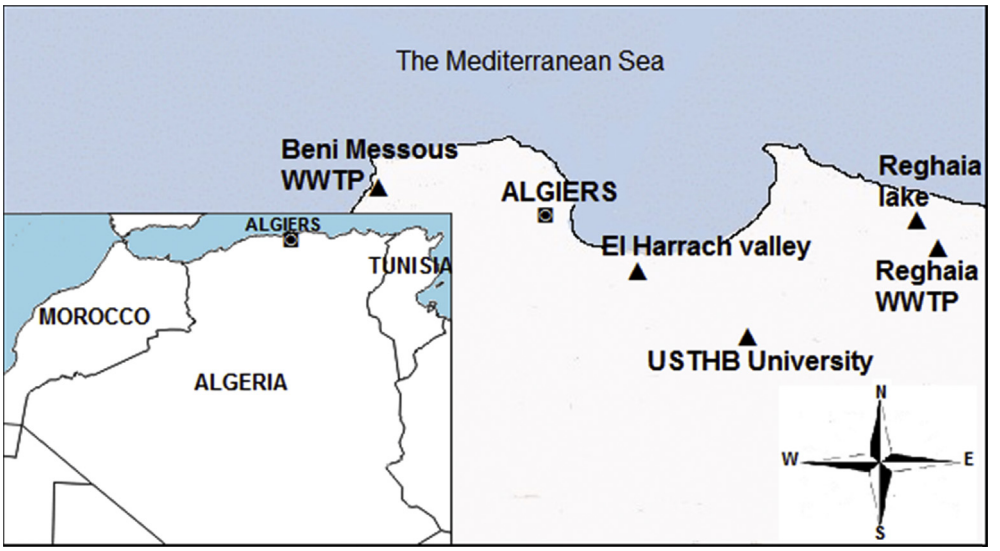


Fig. 1. Map of Algiers, showing the sampling sites [25].

biological treatments and discharges the treated water directly into the Mediterranean Sea.

2.3. Extraction procedures

The extraction procedure was carried out on Oasis® HLB cartridges (60 mg/3 mL). The cartridges were preconditioned with 3 mL of ethyl acetate and 3 mL of ultra-pure water at pH 2.5–3 in sequence. Samples (100 mL for influents, 200 mL for effluents and 300 mL for surface and drinking waters) passed through the SPE cartridges with a flow rate of ~3 mL/min. The cartridges were then rinsed with 3 mL of aqueous methanol (5%) and dried under vacuum for 15 min. Afterwards, they were eluted with 2 mL×3 of ethyl acetate/acetone (50/50; v/v) and collected in 10 mL brown vials. The volume was reduced under nitrogen gas to dryness and then dissolved in 100 µl of ethyl acetate. 1-hydroxypyrene was added to the final extracts for the recovery control. Finally, the derivatization reaction was performed by adding 30 µl of MSTFA, with incubation at 65 °C for 35 min.

2.4. GC–MS analysis

The analysis of the target compounds was realized by GC–MS using an Agilent 7890A GC system connected to 5975C Series MSD with a high-sensitivity triple-axis detector. The separation was carried out in an HP-5 MS capillary column (5% diphenyl/95% dimethylsiloxane; 30 m×0.25 mm×0.25 µm film thickness) connecting the inlet to the MS interface. The carrier gas was ultrapure helium (purity>99.999%, Air Liquide) set at a constant flow mode (1.3 mL/min). 1 µL of the sample extracts was injected into the GC in the splitless mode at 250 °C using an Agilent 7693 Autosampler/G4513A series injector. The GC oven temperature program was set at 70 °C (2 min), and then increased to 280 °C at a rate of 10 °C/min and maintained for 5 min at that temperature (see Table 1).

2.5. Method verification

2.5.1. GC–MS parameters

The target pharmaceutical compounds were first identified in the full-scan mode (m/z 40–550) by direct injection of individual standard solutions, and then a solution of mixed standards. The retention times and m/z ratios for trimethylsilyl (TMS) derivatives are presented in Table 2.

The method verification was performed by optimizing different parameters: linearity, repeatability, accuracy, recovery and method detection/quantification limits.

Isotope-labelled standard ibuprofen-d_3 is absent in the environment but commercially available. It was used as a surrogate standard to calibrate and compensate the experimental losses.

The linearity ranges of the four pharmaceutical compounds were calculated and calibrated, based on the ratio of the peak areas of analytes and the internal standard with five-point calibration curves in the range of 10–2000 ng/L, except for naproxen (100–2000 ng/L). The calibration curves show a good linearity with a high correlation coefficient ($R^2 > 0.99$) (Table 2).

The relative response factor (RRF) and the concentration of individual analytes were determined from the slope of the linear plot using the following equation:

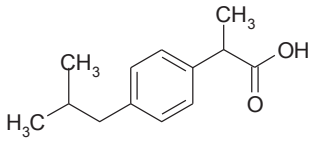
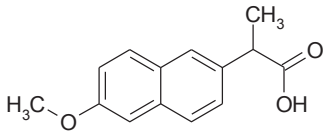
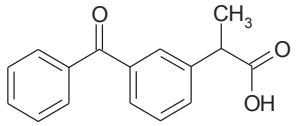
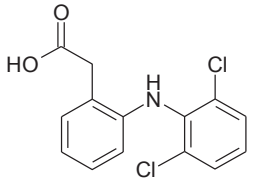
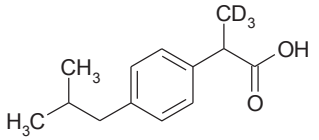
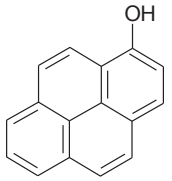
$$CA = \frac{Analyte\ area}{I.S.\ area} \times \frac{CI.S}{RRF} \quad (1)$$

where CA is the concentration of the analyte (ng/L), $I.S$ is the internal standard and $CI.S$ is its concentration (ng/L) [26].

2.5.2. Recovery

For the recovery experiments, 100 mL of filtered effluent water were spiked with 100 ng of ibuprofen-d_3 and 100 ng of each target analyte. The solutions were treated using the same procedure described in Section 2.1. The recoveries

Table 1
Formulae and chemical structures of analytes and deuterated standards.

Compounds	CAS number	Molecular formula	MW (g/mol)	Chemical stricture
Ibuprofen (IBU)	15687-27-1	$C_{13}H_{18}O_2$	206	
Naproxen (NAP)	22204-53-1	$C_{14}H_{14}O_3$	230	
Ketoprofen (KET)	22071-15-4	$C_{16}H_{14}O_3$	254	
Diclofenac (DIC)	15307-79-6	$C_{14}H_{11}C_{l2}NO_2$	296	
Ibuprofen-d_3 (IBU-d3)	121662-14-4	$C_{13}D_3H_{15}O_2$	209	
1-Hydroxypyren (HPY)	5315-79-7	$C_{16}H_{10}O$	218	

were determined by comparing the ratio of the target compounds and internal standard in pre-spiked and post-spiked samples, using the next equation:

$$RE(\%) = \frac{A}{B} \times 100 \quad (2)$$

A and B are the peak areas of the analyte in the sample spiked with the target compounds before and after extraction, respectively.

2.5.3. Matrix effects

The matrix effect was evaluated from the following equation:

$$\text{matrix effect}(\%) = \left[\frac{A_m - A_{m0}}{A_0} - 1\right] \times 100 \quad (3)$$

where A_m, A_{mo} and A_o are the peak areas of the analyte in the spiked sample matrix, the analyte in the unspiked sample and in ultrapure water, respectively [27,28].

Table 2
Method validation of data in terms of calibration results, LODs, LOQs, precision, and accuracy ($n = 3$).

Therapeutic group	Analyte	Retention time (min)	m/z ratio	Recovery % (RSD %)	Matrix effects	LOD ng/L	LOQ ng/L	r^2
Non-steroidal anti-inflammatories	IBU	13.188	160	119 (3)	23	0.5	1.5	0.9985
	NAP	17.960	185	120 (12)	28	16.4	54.5	0.9974
	KET	19.099	282	82 (19)	61	0.5	1.6	0.9950
	DIC	19.923	214	101 (17)	−48	3.3	11	0.9982
Deuterated standard for quantification	IBU-d3	13.188	163					
Standard for recovery validation	HPY	21.395	290					

LOD: limit of detection; LOQ: limit of quantification; SD: standard deviation; RSD: relative standard deviation.

2.5.4. Removal efficiency

The removal efficiency of the four pharmaceuticals were calculated for the WWTPs as the difference between the mean concentrations in influent and effluent samples taken simultaneously. It was determined from the following equation:

$$\text{Removal efficiency } (\%) = \frac{C_{inf} - C_{eff}}{C_{inf}} \times 100 \quad (4)$$

where C_{inf} and C_{eff} are the mean concentrations in influent and effluent wastewaters, respectively; the results are presented in Table 3.

3. Results and discussion

3.1. Recovery, accuracy and detection limits

Extraction experiments showed good recovery values for the selected pharmaceuticals, from 82% for ketoprofen to 120% for naproxen, with an average of 106%. Each analyte was tested in triplicate and the results are presented in Table 2. Recoveries above 100% are not rare in the literature for pharmaceutical compounds and can be found in many studies in the methods developed using polymer adsorbents like Oasis® HLB cartridges [8,20,24]. The high extraction efficiency for polar materials by using the sorbent can cause matrix interferences in the analyses by GC/MS, which is the root of recoveries above the scale [24]. The accuracy was determined by the calculation of analyte recovery relative standard deviation (RSD). Experiments showed a good accuracy and repeatability with relative standard deviations ($\leq$20%) for all the tested pharmaceuticals.

The limit of detection (LOD) and limit of quantification (LOQ) were determined as the minimum detection concentration for the first one and minimum quantification concentration for the second one, that give signal-to-noise ratios (S/N) of 3 and 10, respectively (Table 2). The values of LODs are in the range of 0.45–16.35 ng/L, while the corresponding LOQ values vary between 1.5 and 54.5 ng/L.

3.2. Matrix effects

The matrix effects are calculated using Eq. (3). It is considered that 0% of ME means no matrix interferences with the signal of the target analyte; positive values indicate signal enhancement while negative values represent a signal suppression due to the sample matrix [27].

The results presented in Table 2 show that the matrix effects vary from 23 to 61% for ibuprofen, naproxen, and ketoprofen, causing a signal enhancement, whereas for the diclofenac matrix a signal suppression was caused with a value of −48%. Such results confirm that the matrix does not lead to any significant effect on the signal. GC–MS analysis has less problems with matrix effect suppression or enhancement of the signal but suffers from accumulation of non-volatile matrix components in the GC system and/or signal enhancement caused by the blockage of active sites in the injector influenced by the matrix [28].

3.3. Occurrence in wastewaters and removal efficiency

The concentrations of the selected pharmaceutical compounds in the samples collected from WWTPs are presented in Table 3. This study has shown that all the investigated samples contain pharmaceutical residues. Naproxen is present in Reghaia WWTP influent with the highest concentration of 9.58 μg/L, and a similar concentration of ibuprofen was found in Beni Messous influent (8.613 μg/L). By contrast, in effluents their concentrations were significantly smaller depending on their removal efficiencies. The high concentrations of ibuprofen and naproxen in effluents are the consequence of the wide consumption of these molecules with or without prescription leading to their permanent presence in the effluents, which is considered as pseudo-persistence because of their continual discharge [29]. The consumed ibuprofen, naproxen, ketoprofen and diclofenac are eliminated with 10, 70, 80 and 10% of unchanged drugs, respectively, [30] and their degradation in WWTPs depends on the biological treatment efficiency [8]. Ketoprofen was not detected in the Reghia WWTP but its concentration was increased in the Beni messous WWTP simultaneously with diclofenac, involving negative values for their removal efficiencies.

Increased concentrations were observed for both diclofenac and ketoprofen in the final effluent of the Beni Messous WWTP compared with influent concentrations (Table 3). Similar results indicated that pharmaceutical concentrations in effluent were higher than those encountered in influent as reported in other studies [31–34]. This augmentation is probably due to the deconjugation of conjugated metabolites during the treatment process; an underestimation of the current amount is due to particulate matter with adsorbed pharmaceuticals being filtered out during the sample preparation, and/or the

Table 3
Concentration mean (SD) and removal efficiency of NSAIDs ($n = 3$).

Analyte	Reghaia WWTP			Beni Messous WWTP		
	Influent ng/L (SD ng/L)	Effluent ng/L (SD ng/L)	Removal efficiency (%)	Influent ng/L (SD ng/L)	Effluent ng/L (SD ng/L)	Removal efficiency (%)
IBU	1607.8 (42)	341.4 (26)	78.8	8612.9 (65.5)	431.3 (9)	95
NAP	9584.8 (221.2)	nd	—	1219.7 (6.6)	333.7 (20.4)	72.6
KET	nd	nd	—	565.2 (8.2)	1034.5 (5.7)	−83
DIC	2318.5 (87.3)	1615.7 (136.6)	30.3	990.5 (54.6)	2710.7 (64.2)	−173.7

nd: not detected; SD: standard deviation.

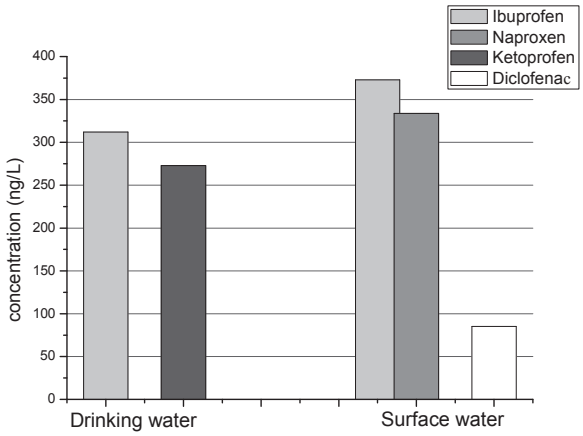


Fig. 2. Presence of PhACs in tap water and surface water.

desorption of PhACs from the particulate phase during the wastewater treatment [32].

A high removal efficiency was observed for ibuprofen in the Beni Messous WWTP (95%), while low removal yields were obtained for diclofenac (30.3%) in the Reghaia WWTP. The removal efficiency depends on several factors like the chemical structure and properties of the pharmaceutical compounds, the specific treatment processes employed by individual WWTPs and/or the wastewater residence time at different WWTPs [32,35].

The introduction of effluents containing pharmaceutical compounds in the aquatic medium presents high risks for the aquatic living organisms, depending on the dilution phenomena, that is, high in the open aquatic systems and low in the semi-open and closed aquatic systems [8]. These molecules exert biological effects on people or animals and may have a chronic impact on the toxicity of aquatic living organisms [36]. Such organisms are captive to the continual cycle-life because effects could accumulate so slowly that a major change becomes undetected until the cumulative level of these effects, multigenerational exposure [37].

3.4. Occurrence in surface water and drinking water

The concentrations of the selected pharmaceuticals in tap drinking water and surface water are illustrated in Fig. 2. The pharmaceutical concentrations were remarkably low compared to those encountered in wastewaters. In tap water, ibuprofen and ketoprofen were present at concentrations of 312.1 and 273 ng/L, respectively, while naproxen and diclofenac were not detected. On the other hand, the pharmaceutical concentrations in the surface water were found to be 85.2 ± 9.3 ng/L for diclofenac, 372.8 ± 19.8 ng/L for ibuprofen and 334 ± 15.2 ng/L for naproxen, while ketoprofen was not detected. Mainly, the major source of PhACs could be considered as WWTP discharges. The most detected pharmaceuticals in the surface water are the most occurred pharmaceuticals in the WWTP effluents. Their concentrations were decreased along the distance affected by natural dilution. On the other side, the behaviour of these pharmaceuticals in surface and drinking waters is very similar to their behaviour in the influents, which involves a relationship to a direct discharge of untreated wastewaters into the aquatic environment. In this case, the pharmaceutical compounds exist as a mixture of many different therapeutic groups, in addition to their metabolites. They can present synergic and additive effects, and consequently a higher toxicity [38].

3.5. Comparison with other studies

A comparison with different studies around the world is reported (Table 4). In this study, the concentrations of pharmaceutical residues in Algiers WWTP influent range from not detected (nd) to 9585 ng/L and the concentrations vary in other countries. However, for ibuprofen, the concentration found in our case is four times less than in Spain [29]. In the effluents, the concentrations increase from 334 to 1035 ng/L concerning ibuprofen, naproxen, and ketoprofen. These values are in the range reported in the cited studies, contrarily to diclofenac, whose concentration is above 2711 ng/L.

In our investigation, ketoprofen was not detected in the surface water while the other pharmaceutical's concentrations (ibuprofen, naproxen, and diclofenac) in Algiers surface water are in the same range to those reported in the European countries. Their concentrations in France and Asian countries were lower compared with our results.

In this study, naproxen and diclofenac were not detected in drinking water. The concentrations of ibuprofen and ketoprofen were relatively low compared with those encountered in the USA, whereas high concentrations were detected in comparison with those found in Canada, China and some European countries. This is possibly due to the incomplete removal of these compounds in WWTPs. The high consumption of some compounds without prescription and the direct discharge of wastewater into the aquatic systems without processing by WWTPs (industry, agriculture and the other sources) are mainly responsible for this pollution. These factors make their control and elimination somewhat delicate.

4. Conclusions

An analytical method based on Solid Phase Extraction (SPE) followed by gas chromatography separation coupled with mass spectrometry detection was verified for the analysis and determination of four non-steroidal anti-inflammatory drugs in surface water, drinking water and wastewaters in Algiers.

The derivatization reaction of individual pharmaceutical compounds into trimethylsilyl derivatives with MSTFA has improved their volatility and thermal stability, making their analysis and determination more suitable via gas chromatography/mass spectrometry.

Satisfactory recoveries (between 82 and 120%) were obtained for the target compounds with good repeatability as confirmed by the low relative standard deviations and quantification limits in the ranges comparable with other studies.

Table 4
Comparison with different studies in the world (ng/L).

Location	IBU	NAP	KET	DIC	References
WWTP Influent					
Canada	4100–10,210	1730–6030	60–0150	50–2450	[39]
Germany	600–1660			nd–1230	[40]
Belgium	5711–7847	2374–4110		507–1450	[34]
Italy	6624	1079	250	1020	[41]
Sweden	751.3	5153		110.7	[19]
Sweden	3590	3650	940	160	[42]
Spain	39,800	3580	1170	1490	[29]
Spain	<LOQ-4113	1196–5228	<LOQ-801	<LOQ-561	[43]
Poland	280	240	<MDL	460	[18]
Portugal	1596 ± 1715	741 ± 522	458 ± 112	69.7 ± 89.4	[44]
Algeria	1608–8613	1220–9585	nd–565	991–2319	This study
WWTP Effluent					
Canada	110–2170	360–2540	40–90	70–250	[39]
UK	2203	856		459	[24]
Germany	3400	520	380	2100	[45]
France	17.7–219.0	42.1–289.1	21.8–1080.6	210.7–486.4	[8]
Belgium	<LOQ	<LOQ		542–1391	[34]
Italy	1003	526	175	507	[41]
Sweden	14.1	32.1		33.3	[19]
Sweden	150	250	330	120	[42]
Spain	<LOQ	0.72	0.62	0.74	[29]
Spain	<LOQ-653	359–2208	277–539	6–431	[43]
Serbia	20,130	208	247	1338	[46]
Poland	110	70	<MDL	120	[18]
Portugal	119 ± 136	303 ± 275	218 ± 52	42.9 ± 19.5	[44]
Taiwan	<12–34		330–700	<2–30	[9]
Algeria	341–431	nd–334	nd–1035	1616–2711	This study
Drinking water					
USA	510–1350				[47]
Canada	25				[48]
France	nd–0.6	nd–0.2	nd–3.0	nd–2.5	[8]
Spain	39	11		18	[35]
Serbia			16		[46]
China	77	96	50	80	[23]
Algeria	312		273		This study
Surface water					
UK	52	104		305	[24]
France	nd–24	nd–24	nd–23	<LOQ-41	[36]
Germany	530	390	120	1200	[45]
Italy	95–210	200–264	nd–150	nd–120	[41]
Spain	2234–16,886	387–3140	43–1567	313–3363	[49]
Spain	830	278		49	[35]
Serbia	<LOQ-346	<LOQ-74.2	45	<LOQ-324	[46]
China	23.3	12.3	28.6	13.6	[50]
China	54	72	77	63	[23]
S. Korea	1.2–51	5.3–100		0.87–30	[51]
Algeria	373	334		85	This study

All studied compounds were detected in WWTP influents and effluents water with different concentrations (334–9585 ng/L) and confirm the incapability of classical WWTPs to remove completely this kind of emerging contaminants. The presence of some studied compounds (ibuprofen, naproxen, and diclofenac) in surface water and (ibuprofen and ketoprofen) in tap water is not only due to WWTP's less efficiency. Other sources like industry and agriculture are also responsible for such contamination without processing by WWTPs.

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